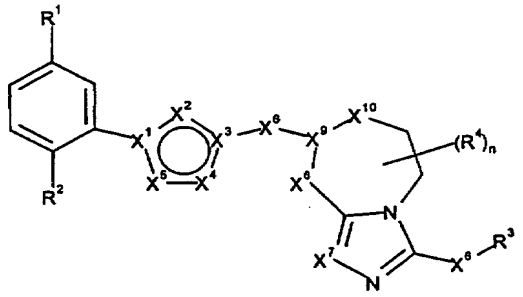
CLAIMS

1. A compound of formula I:



(I)

wherein

X^1, X^2, X^3, X^4, and X^5 are independently selected from the group consisting of C, CR^5, N, O, and S, wherein at least one of X^1, X^2, X^3, X^4, and X^5 is not N;

X^6 is selected from the group consisting of a bond and CR^5R^6;

X^7 is CR^5 or N;

X^8 is selected from the group consisting of a bond, CR^5R^6, NR^5, O, S, SO, and SO_2;

X^9 is CR^5 or N;

X^{10} is selected from the group consisting of a bond, CR^5R^6, $(CR^5R^6)_2$, O, S, and NR^5;

R^1 is selected from the group consisting of hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$, C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

R^2 is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}

$_{6}$alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$,C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

R^3 is a 5- or 6-membered ring containing atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

R^4 is selected from the group consisting of hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^6, OC_{2-6}alkylNR^5R^6, C_{1-6}alkyl$(CO)NR^5R^6$, OC_{1-6}alkyl$(CO)NR^5R^6$, C_{0-6}alkyl$NR^5(CO)R^6$, OC_{2-6}alkyl$NR^5(CO)R^6$, C_{0-6}alkyl$NR^5(CO)NR^5R^6$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^6$, OC_{2-6}alkyl$(SO_2)NR^5R^6$,C_{0-6}alkyl$NR^5(SO_2)R^6$, OC_{2-6}alkyl$NR^5(SO_2)R^6$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^6$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^6$, $(CO)NR^5R^6$, $O(CO)NR^5R^6$, NR^5OR^6, C_{0-6}alkyl$NR^5(CO)OR^6$, OC_{2-6}alkyl$NR^5(CO)OR^6$, SO_3R^5 and a 5- or 6-membered ring containing atoms independently selected from the group consisting of C, N, O and S, wherein said ring may be substituted by one or more A;

R^5 and R^6 are independently selected from the group consisting of hydrogen, C_{1-6}alkyl, C_{3-7}cycloalkyl and aryl;

A is selected from the group consisting of hydrogen, hydroxy, halo, nitro, C_{1-6}alkylhalo, OC_{1-6}alkylhalo, C_{1-6}alkyl, OC_{1-6}alkyl, C_{2-6}alkenyl, OC_{2-6}alkenyl, C_{2-6}alkynyl, OC_{2-6}alkynyl, C_{0-6}alkylC_{3-6}cycloalkyl, OC_{0-6}alkylC_{3-6}cycloalkyl, C_{0-6}alkylaryl, OC_{0-6}alkylaryl, CHO, $(CO)R^5$, $O(CO)R^5$, $O(CO)OR^5$, $O(CN)OR^5$, C_{1-6}alkylOR^5, OC_{2-6}alkylOR^5, C_{1-6}alkyl$(CO)R^5$, OC_{1-6}alkyl$(CO)R^5$, C_{0-6}alkylCO_2R^5, OC_{1-6}alkylCO_2R^5, C_{0-6}alkylcyano, OC_{2-6}alkylcyano, C_{0-6}alkylNR^5R^5, OC_{2-6}alkylNR^5R^8, C_{1-6}alkyl$(CO)NR^5R^8$, OC_{1-6}alkyl$(CO)N\ R^5R^8$, C_{0-6}alkyl$NR^5(CO)R^8$, OC_{2-6}alkyl$NR^5(CO)R^8$, C_{0-6}alkyl$NR^5(CO)N\ R^5R^8$, C_{0-6}alkylSR^5, OC_{2-6}alkylSR^5, C_{0-6}alkyl$(SO)R^5$, OC_{2-6}alkyl$(SO)R^5$, C_{0-6}alkylSO_2R^5, OC_{2-6}alkylSO_2R^5, C_{0-6}alkyl$(SO_2)NR^5R^8$, OC_{2-6}alkyl$(SO_2)NR^5R^8$,C_{0-6}alkyl$NR^5(SO_2)R^8$, OC_{2-6}alkyl$NR^5(SO_2)R^8$, C_{0-6}alkyl$NR^5(SO_2)NR^5R^8$, OC_{2-6}alkyl$NR^5(SO_2)NR^5R^8$,

$(CO)NR^5R^8$, $O(CO)NR^5R^8$, NR^5OR^8, $C_{0-6}alkylNR^5(CO)OR^8$, $OC_{2-6}alkylNR^5(CO)OR^8$, SO_3R^5 and a 5- or 6-membered ring containing atoms independently selected from the group consisting of C, N, O and S;

n is 0, 1, 2, 3, or 4; or
a pharmaceutically acceptable salt or hydrate thereof;

provided that:

a)when X2 = X4 = X5 = N, and either of X8 or X10 is a bond, then X9 is not N,

b) when X^7 is N at least two of X^1, X^2, X^3, X^4, and X^5 are not N,

c) X^1 and X^3 are not O;

and provided that the compound is not:

8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridine-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,
8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-thiophen-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyridine,
8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridine-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyridine,
8-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-pyridine-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,
8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3ylmethyl]-3-pyridine-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,
8-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-ylmethyl]-3-pyridine-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,
8-{1-[5-(3-Chloro-phenyl)-[1,3,4]oxadiazol-2-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,
8-[5-(5-Chloro-2-fluoro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,
8-{1-[5-(3-Chloro-phenyl)-[1,2,4]oxadiazol-3-yl]-ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,
3-Pyridin-4-yl-8-[1-(5-m-tolyl-[1,2,4]oxadiazol-3-yl)-ethyl]-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,
(+)-8-{(1S)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine,
(-)-8-{(1R)-1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-5,6,7,8-tetrahydro[1,2,4]triazolo[4,3-a]pyrimidine,
3-[5-(3-Pyridin-4-yl-6,7-dihydro-5*H*-[1,2,4]triazolo[4,3-*a*]pyrimidin-8-ylmethyl)[1,3,4]oxadiazol-2-yl]benzonitrile,
3-{5-[3-(2-Methoxypyridin-4-yl)-6,7-dihydro-5*H*-[1,2,4]triazolo[4,3-*a*]pyrimidin-8-ylmethyl][1,3,4]oxadiazol-2-yl}benzonitrile,
3-{5-[3-(2-Methoxy-pyridin-4-yl)-6,7-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrimidin-8-ylmethyl]-[1,2,4]oxadiazol-3-yl}-benzonitrile,

3-{3-[(3-pyridin-4-yl-6,7-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-8(5*H*)-yl)methyl]-1,2,4-oxadiazol-5-yl}benzonitrile,
3-(3-{[3-(2-methoxypyridin-4-yl)-6,7-dihydro[1,2,4]triazolo[4,3-*a*]pyrimidin-8(5*H*)-yl]methyl}-1,2,4-oxadiazol-5-yl)benzonitrile,
3-{5-[(3-pyridin-4-yl-6,7-dihydro[1,2,4]triazolo[4,3-a]pyrimidin-8(5H)-yl)methyl]-1,2,4-oxadiazol-3yl}benzonitrile, and
3-{5-[3-(2-Hydroxy-pyridin-4-yl)-6,7-dihydro-5H-[1,2,4]triazolo[4,3-a]pyrimidin-8-ylmethyl]-[1,2,4]oxadiazol-3-yl}-benzonitrile.

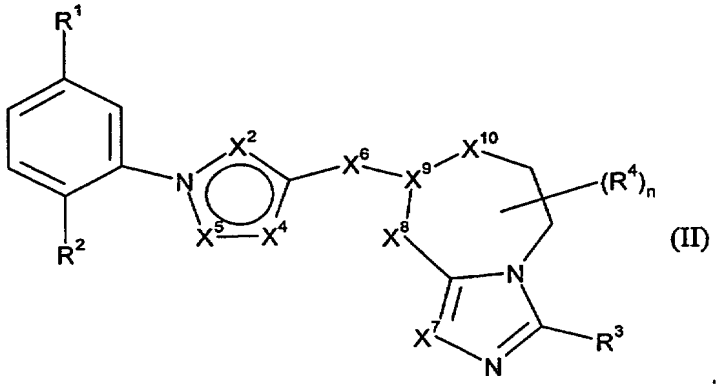
2. The compound according to claim 1, provided that the compound is not 8-[5-(5-Chloro-phenyl)-[1,2,4]oxadiazol-3-ylmethyl]-3-furan-2-yl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrimidine,

3. The compound according to claim 1, wherein R^1 is halo, $C_{1\text{-}6}$alkylhalo, $C_{1\text{-}6}$alkyl, $OC_{1\text{-}6}$alkyl, or $C_{0\text{-}6}$alkylcyano.

4. The compound according to claim 1, wherein R^2 is hydrogen or halo.

5. The compound according to claim 1, wherein R^2 is fluorine.

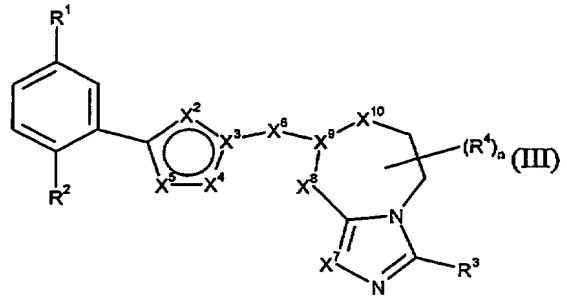
6. The compound according to claim 1, of Formula II:



(II)

7. The compound according to claim 6, wherein X^7 is N.

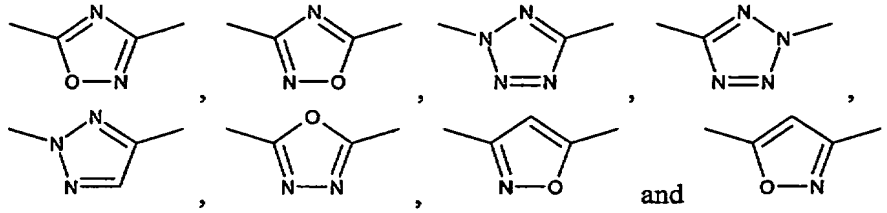
8. The compound according to claim 1, of Formula III:


(III)

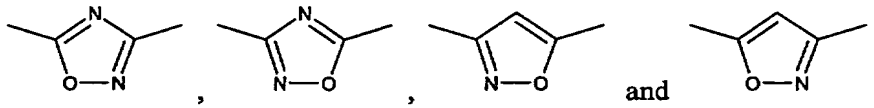
9. The compound according to claim 8, wherein X^3 is C.

10. The compound according to claim 8, wherein X^3 is N.

11. The compound according to claim 1, wherein the ring containing X^1, X^2, X^3, X^4, and X^5 is selected from the group consisting of:


and

12. The compound according to claim 11, wherein the ring is selected from the group consisting of:


and

13. The compound according to claim 11, wherein X^7 is N.

14. The compound according to claim 13, wherein X^8 is a bond.

15. The compound according to claim 13, wherein X^8 is S.

16. The compound according to claim 14, wherein X^9 is CR^5.

17. The compound according to claim 16, wherein X^{10} is NR^5.

18. The compound according to claim 16, wherein X^{10} is O.

19. The compound according to claim 16, wherein X^{10} is CR^5R^6.

20. The compound according to claim 16, wherein X^{10} is $(CR^5R^6)_2$.

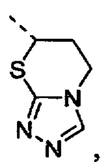
21. The compound according to claim 16, wherein X^{10} is a bond.

22. The compound according to claim 15, wherein X^9 is CR^5.

23. The compound according to claim 22, wherein X^{10} is a bond.

24. The compound according to claim 14, wherein X^9 is N.

25. The compound according to claim 11, wherein the fused ring containing X^7, X^8, X^9, and X^{10} is selected from the group consisting of: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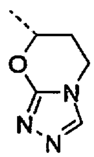
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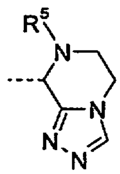
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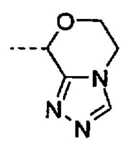
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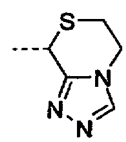
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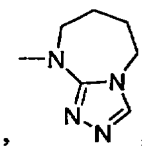
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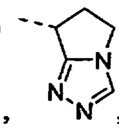
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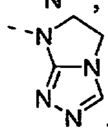
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26. The compound according to claim 1 selected from the group consisting of:
7-[5-(5-Chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]-3-(2-thienyl)-6,7-dihydro-5H-[1,2,4]triazolo[3,4-b][1,3]thiazine,
9-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-3-pyridin-4-yl-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine,
9-{1-[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]ethyl}-3-pyridin-4-yl-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine,
7-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-3-pyridin-4-yl-6,7-dihydro-5H-pyrrolo[2,1-c][1,2,4]triazole,
9-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-3-(trifluoromethyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine,
8-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-3-(4-methoxy-phenyl)-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine,
8-[3-(3-Chloro-phenyl)-[1,2,4]oxadiazol-5-yl]-3-(4-methoxy-phenyl)-7-methyl-5,6,7,8-tetrahydro-[1,2,4]triazolo[4,3-a]pyrazine,
9-{[5-(3-chlorophenyl)isoxazol-3-yl]methyl}-3-(3,5-difluorophenyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine,
9-{[5-(3-chlorophenyl)isoxazol-3-yl]methyl}-3-(4-methoxyphenyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine,
9-{[5-(3-chlorophenyl)isoxazol-3-yl]methyl}-3-pyridin-4-yl-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine,

9-{[5-(5-chloro-2-fluorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-3-pyridin-4-yl-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine,

9-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-3-(3,5-difluorophenyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine,

9-{[5-(3-chlorophenyl)-1,2,4-oxadiazol-3-yl]methyl}-3-(4-methoxyphenyl)-6,7,8,9-tetrahydro-5H-[1,2,4]triazolo[4,3-a][1,3]diazepine, and

pharmaceutically acceptable salts thereof.

27. A pharmaceutical composition comprising as active ingredient a therapeutically effective amount of the compound according to any one of claims 1-26, and one or more pharmaceutically acceptable diluents, excipients, and/or inert carriers.

28. The pharmaceutical composition according to claim 27, for use in the treatment of mGluR5-mediated disorders.

29. The compound according to any one of claims 1-26, for use in therapy.

30. The compound according to any one of claims 1-26, for use in the treatment of mGluR5-mediated disorders.

31. Use of the compound according to any one of claims 1-26 in the manufacture of a medicament for the treatment of mGluR5-mediated disorders.

32. A method for the treatment of mGluR5-mediated disorders, comprising administering to a mammal a therapeutically effective amount of the compound according to any one of claims 1-26.

33. The method according to claim 32, wherein the mammal is a human.

34. The method according to claim 32, wherein the disorder is a neurological disorder.

35. The method according to claim 32, wherein the disorder is a psychiatric disorder.

36. The method according to claim 32, wherein the disorders are selected from chronic and acute pain disorders.

37. The method according to claim 32, wherein the disorder is a gastrointestinal disorder.

38. A method for inhibiting activation of mGluR5 receptors, comprising contacting a cell containing said receptors with an effective amount of a compound according to any one of claims 1-26.